UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,501	02/09/2004	Leena Peltonen	021825-006300US	2308

20350 7590 08/18/2011

KILPATRICK TOWNSEND & STOCKTON LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
JOHANNSEN, DIANA B	

ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
08/18/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

Docket@kilpatricktownsend.com
ipefiling@kilpatricktownsend.com
jlhice@kilpatrick.foundationip.com

Office Action Summary	Application No.	Applicant(s)
	10/775,501	PELTONEN ET AL.
	Examiner	Art Unit
	DIANA JOHANNSEN	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *41,43,44,48,51,52,56,75-77,79-82 and 86-102* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48,51,52 and 86* is/are allowed.

6)☒ Claim(s) *41,43,44,48,56,75,77,79-82 and 87-102* is/are rejected.

7)☒ Claim(s) *76* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)	
1) ☐ Notice of References Cited (PTO-892)	4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐ Notice of Informal Patent Application
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114 was filed in this application after appeal to the Board of Patent Appeals and Interferences, but prior to a decision on the appeal. Since this application is eligible for continued examination under 37 CFR 1.114 and the fee set forth in 37 CFR 1.17(e) has been timely paid, the appeal has been withdrawn pursuant to 37 CFR 1.114 and prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on November 29, 2010 has been entered.

2. Claims 41, 48, 77, and 86 have been amended, claims 83-85 have been canceled, and claims 87-102 have been added. All pending claims (41, 43-44, 48, 51-52, 56, 75-77, 79-82, and 86-102) are now under consideration. Claims 48, 51-52, and 86 are allowed, and claim 76 is objected to but is directed to allowable subject matter (see below). The remaining claims, while free of the prior art, are rejected for the reasons set forth below.

Election/Restrictions

3. Because claims directed to the elected species of SEQ ID NO: 5 are now free of the prior art, search and examination has been extended to SEQ ID NO: 3, as well as combinations of SEQ ID NOS 5 and 3. It is noted that applicants claims directed to combinations of nucleic acids including portions of SEQ ID NOS 5 and 3 including position 324, while rejected on other grounds, are free of the prior art. Accordingly, in the interest of compact prosecution, and because applicants composition and method

claims appear to embrace related allowable subject matter, the new method claims 97-102 have been rejoined and examined with the product claims under consideration herein. In view of the rejoinder of the method claims, **the restriction requirement as set forth in the Office action mailed on October 11, 2006 is hereby withdrawn with regard to elected Group I and Group VII (i.e., the group to which the methods of current claims 97-102 correspond)** . In view of the withdrawal of the restriction requirement as to the rejoined inventions, applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Once the restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

Allowable Subject Matter

4. Claims 48, 51-52, and 86 are allowed. The prior art does not teach or suggest the particular nucleic acid molecules present in the vectors/cells of claims 48 and 51-52, or in the kit of claim 86. As discussed previously on the record, the closest prior art reference, Birren et al, teaches a *H. sapiens* chromosome 2 clone including a sequence that is identical to SEQ ID NO: 5 with the exception of 3 mismatches; this sequence contains 4 mismatches with respect to instant SEQ ID NO: 3 (specifically, the 3 mismatches of SEQ ID NO: 5 and the additional mismatch at position 324, i.e., at the position established in the instant specification as corresponding to a SNP

associated with lactose intolerance; see alignment at the end of this Office action). The prior art did not disclose the products of the instant claims and did not provide any motivation to prepare these specific nucleic acid molecules (or vectors including them).

5. Claim 76 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. It is noted that product of claim 41 (from which claim 76 depends) is also allowable subject matter; however, the claim is considered indefinite with respect to the embodiments specified in dependent claims 42-43 (see rejection below).

Specification

6. The disclosure is objected to because of the following informalities: a separate section corresponding to a "Brief Description" of the Figures/Drawings is lacking. This objection may be overcome by inserting an appropriate heading on page 23 prior to line 5. Appropriate correction is required.

Claim Rejections - 35 USC § 112, second paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 41, 43-44, 79, 87-88, 90, 94-95, and 97-102 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is noted that the definiteness of the claims has been re-evaluated in view of the *Supplementary Examination Guidelines for Determining Compliance with 35 USC*

112 and for Treatment of Related Issues in Patent Applications (76 Fed.Reg. 7162 [09 Feb 2011]).

Claims 41 and 43-44 are indefinite over the recitation of the limitations "wherein said nucleic acid molecule is genomic DNA" in claim 43 and "wherein said genomic DNA is part of a gene" in claim 44. This rejection applies to claim 41 to the extent that that claim is drawn to the embodiments of dependent claims 43-44. It is unclear how the requirement for the nucleic acid molecule to be "genomic DNA" and "part of a gene" actually further limits that which is claimed. Neither the specification nor the prior art provide guidance with regard to what additional characteristics or features would be present in the molecules of claims 43-44 as compared to the molecules defined as in claim 41. Accordingly, additional clarification is required.

Claim 79 is indefinite because it is unclear how the claim further limits claim 77, from which it depends. Claim 79 is drawn to the "nucleic acid molecule of claim 77, wherein said sequence consists of from 14 to 24 nucleotides." It is noted that claim 77 is directed to a molecule "comprising a sequence of at least 14 consecutive nucleotides of SEQ ID NO: 3....", and that claim 79 is further limiting of "said sequence" rather than of, e.g., "said molecule". Because claim 77 is directed to a molecule "comprising" the sequence, it is unclear how the further requirement of claim 79 actually further limits the molecule claimed in claim 77. For example, while the "comprising" language of claim 77 would appear to allow the claim to broadly encompass any molecule including any 14-24 contiguous nucleotides of SEQ ID NO: 3, at least some of these embodiments would include sequences flanking the "14-24 contiguous nucleotides"

that are also present within SEQ ID NO: 3 (and it is unclear whether such molecules are or are not embraced by the claim). Further, it appears that claim 79 may have been intended as a further limitation pertaining to the claimed "molecule" rather than the "sequence" present therein (as the claim does not explicitly reference, e.g., 14-24 contiguous nucleotides of SEQ ID NO: 3, etc.). Accordingly, clarification is required.

Claims 87-88 are indefinite over the limitations "wherein said nucleic acid molecule is a primer" and "wherein said nucleic acid molecule is a probe," respectively. Neither the specification nor the prior art provides clear guidance with regard to how a molecule such as that of claim 77 that "is a primer" or "is a probe" would differ from the molecule of claim 77 itself, and the claim itself does not specify any further requirements of such molecules that makes the further requirements of claims 87 and 88 clear. More particularly, it is noted that while the specification discusses preferred lengths for primers (see page 11), there is no definition in the specification (or in the art) that makes clear how one of ordinary skill would differentiate between molecules included by and excluded from claim 87. Similarly, while the specification and art disclose that, e.g., labeled nucleic acid molecules may be employed as probes (see pages 17-19), unlabeled molecules may also be so employed, and the specification does not state any specific requirements that would allow one of ordinary skill to recognize what molecules are included by and excluded from claim 88. Accordingly, further clarification is required.

Claim 90 is indefinite because it is unclear how the claim further limits claim 89, from which it depends. As discussed above with regard to claim 79, claim 90 is

similarly further limiting of "each of said first and second sequences" of claim 89. However, claim 89 is directed to a composition comprising first and second nucleic acid molecules "comprising" first and second sequences "at least 14 consecutive nucleotides of SEQ ID NO: 3/5....". Claim 90 is further limiting of said first/second "sequence" rather than of, e.g., said first/second molecule. Because claim 89 is directed to molecules "comprising" the referenced sequences, it is unclear how the further requirements of claim 90 actually further limits the molecules claimed in claim 90. For example, while the "comprising" language of claim 89 would appear to allow the claim to broadly encompass any molecule including any 14-24 nucleotides of SEQ ID NO: 3, at least some of these embodiments would include sequences flanking the "14-24 nucleotides" that are also present within SEQ ID NO: 3/5 (and it is unclear whether such molecules are or are not embraced by the claim). Further, it appears that claim 90 may have been intended as a further limitation pertaining to the claimed "molecules" rather than the "sequences" present therein (as the claim does not explicitly reference, e.g., 14-24 contiguous nucleotides of SEQ ID NO: 3/5, etc.). Accordingly, clarification is required.

Claims 94-95 are indefinite over the limitations "wherein each of said first and second nucleic acid molecules is a primer" and "wherein each of said first and second nucleic acid molecules is a probe," respectively. Neither the specification nor the prior art provides clear guidance with regard to how a molecule such as that of claim 89 that "is a primer" or "is a probe" would differ from the molecules of claim 89 itself, and the claim itself does not specify any further requirements of such molecules that makes the

further requirements of claims 94-95 clear. More particularly, it is noted that while the specification discusses preferred lengths for primers (see page 11), there is no definition in the specification (or in the art) that makes clear how one of ordinary skill would differentiate between molecules included by and excluded from claim 94. Similarly, while the specification (and art) disclose that, e.g., labeled nucleic acid molecules may be employed as probes (see pages 17-19), unlabeled molecules may also be so employed, and the specification does not state any specific requirements that would allow one of ordinary skill to recognize what molecules are included by and excluded from claim 95. Accordingly, further clarification is required.

Claims 97-102 are indefinite because it is unclear what is required by the "indicating" of (c) of claim 97. Particularly, it is unclear what types of activities would be considered as "sufficient to meet the "indicating" requirement of the claims, and thus it is unclear what types of methods are embraced by (and excluded from) the claims. Accordingly, additional clarification is required.

Claim 99 is indefinite in requiring that "each of said first and second sequences consists of from 14 to 24 nucleotides." This language is indefinite because it is unclear how it further limits the molecules employed in the method of claim 97, for the same reasons noted above with regard to claim 90 as compared to claim 89.

Claim Rejections - 35 USC § 101

9. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

10. Claims 56, 77, 79, 87-90 and 94-95 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 77, 79, 87-90, and 94-95, as written, do not sufficiently distinguish over nucleic acids as they exist naturally because the claims do not particularly point out any non-naturally occurring differences between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. See *Diamond v. Chakrabarty*, 447 US 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "isolated" or "purified" as in, e.g., claim 41. With particular regard to independent claim 77, it is noted that the claim has been amended to recite a nucleic acid molecule "comprising" a sequence that may include sequences as found in nature, and thus encompasses naturally occurring nucleic acid molecules. With particular regard to independent claim 89, the claim appears to encompass naturally occurring "compositions," particularly those including two nucleic acid molecules that would naturally occur together in cells of a subject heterozygous for the polymorphism that is the subject of the invention. Regarding claim 56 (dependent from claim 77), the requirement that the molecule constitute a "diagnostic composition for diagnosing or assessing an individual's predisposition to develop adult-type hypolactasia" appears to constitute an intended use that does not differentiate the claimed product from the naturally occurring molecule (note, .e.g, the discussion at page 16 of the specification, which references a "diagnostic composition comprising the nucleic acid molecule as described herein"). With further regard to dependent

claims 79, 87-88, 90 and 94-95, it is reiterated that the language of these claims does not clearly differentiate the products claimed from those of the claims from which they depend (claims 79 and 89). This rejection applies to claims 79, 87-88, 90 and 94-95 to the extent that those claims also encompass naturally occurring products (e.g., with regard to claims 79 and 90, molecules that "comprise" sequences consisting of sequences within SEQ ID NO: 3 and flanking sequences also found in SEQ ID NO: 3 such that the molecules are naturally-occurring, and [regarding claims 87-88 and 94-95] naturally occurring molecules that have the capability of functioning in some manner as primers and probes).

Claim Rejections - 35 USC § 112, first paragraph - enablement

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 56, 75, 77, 79-82, and 87-102 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleic acids consisting of fragments of SEQ ID NO: 3 and/or 5 (or the complements thereof) that include at least 14 consecutive nucleotides encompassing position 324 of SEQ ID NO: 3/5 (or the complements thereof), and for isolated nucleic acids comprising sequences of at least 14 consecutive nucleotides of SEQ ID NOs 3/5 including position 324 of SEQ ID NO: 3/5 (or the complements thereof) wherein said isolated nucleic acids hybridize under highly stringent conditions of the particular type specified at page 5, lines 12-15 (including both hybridization and wash conditions) to either SEQ ID NO: 3

or the complement thereof or SEQ ID NO: 5 or the complement thereof, as well as compositions including such nucleic acids, and for methods in which such molecules are employed as probes in a method as specified in claim 97, does not reasonably provide enablement for nucleic acid molecules and compositions thereof as they are broadly claimed herein (claims 77 and 89 and claims dependent therefrom) or for methods employing such nucleic acids as probes in testing for "the presence of or predisposition to adult-type hypolactasia in a subject" (claim 97 and claims dependent therefrom). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)). It is noted that the examiner has considered all of the evidence related to each of these factors, and that those factors, reasons and evidence that

have led to a conclusion that enablement is lacking are discussed below (*MPEP* 2164.04).

Claim 77 and claims dependent therefrom (56, 75, 79-82, and 87-88) are directed to a nucleic acid molecule "comprising a sequence of at least 14 consecutive nucleotides of SEQ ID NO: 3, which includes position 324 of SEQ ID NO: 3, or a sequence of at least 14 consecutive nucleotides of the complementary sequence to SEQ ID NO: 3, which includes position 324 of the complementary sequence. It is noted that dependent claim 56 is directed to a "diagnostic composition for diagnosing or assessing an individual's predisposition to develop adult-type hypolactasia" comprising the molecule of claim 77; neither claim 77 nor any other claim dependent therefrom recites an intended use of the claimed molecule. Claim 89 and claims dependent therefrom (90-96) are directed to a composition comprising a "first nucleic acid molecule" having the same properties as the molecule of claim 77 and a "second nucleic acid molecule comprising a second sequence of at least 14 consecutive nucleotides of SEQ ID NO: 5, which includes position 324 of SEQ ID NO:5, or a sequence of at least 14 consecutive nucleotides of the complementary sequence to SEQ ID NO:5, which includes position 324 of the complementary sequence." It is noted that neither claim 89 nor any claims dependent therefrom recite an intended use of the claimed composition. Claim 97 and claims dependent therefrom are directed to a method "for testing for the presence of or predisposition to adult-type hypolactasia in a subject" comprising "(a) contacting a nucleic acid obtained from said subject" with a composition having the characteristics noted above with regard to claim 89, "(b)

detecting the presence or absence of hybridization between said first and second probes with said nucleic acid obtained from said subject," and "(c) indicating the presence of or predisposition to adult-type hypolactasia in said subject when the presence of hybridization between said second probe with said nucleic acid obtained from said subject is detected in the absence of hybridization between said first probe and said nucleic acid obtained from said subject".

Regarding dependent claim 56 (and claim 77 to the extent drawn to the embodiment of claim 56), *MPEP* 2164.01(c) states that "When a compound or composition claim is limited by a particular use, enablement of that claim should be evaluated based on that limitation." Thus, claim 56 has been evaluated with regard to whether the composition of that claim is enabled "for diagnosing or assessing" as recited in the claim. With regard to claims 77 and 89 and claims dependent therefrom other than claim 56, *MPEP* 2164.01(c) states that "when a compound or composition claim is not limited by a recited use, any enabled use that would reasonably correlate with the entire scope of that claim is sufficient to preclude a rejection for non-enablement based on how to use". Thus, enablement of these product claims has been evaluated with regard to any uses therefore disclosed in the specification. It is additionally noted that 35 USC 112, first paragraph "requires an indication of how the use (required by 35 USC 101) can be carried out" (MPEP 2164.07); thus, the use that must be enabled is one that meets the requirement of being a specific, substantial and credible utility (such as the diagnostic use specified in claim 56, as opposed to a general use that would apply to any nucleic acid molecule). Regarding the method

claims under consideration herein (claims 97-102), the claims have a stated intended use of "testing for the presence of or predisposition to adult type hypolactasia in a subject" and recite a final step of "indicating" the presence of or predisposition to this condition; thus, enablement of the claimed methods requires that one of skill in the art be able to achieve this intended use via the performance of the recited method steps (as stated in the claims themselves) without undue experimentation.

Regarding the products of claims 77 and 89 and claims dependent therefrom, the specification discloses that the nucleic acids of the invention contribute to or are indicative of adult-type hypolactasia (i.e., lactose intolerance) (see, e.g., page 4) and discloses the use of such nucleic acids in testing for lactose intolerance or the absence thereof (see, e.g., pages 7-9; 16-18). The specification teaches the use of nucleic acids of the invention as primers in detecting of the SNP(s) indicative of lactose intolerance (pages 11-12)(i.e., another diagnostic use). The specification also asserts that the nucleic acid molecules of the invention may be used in gene therapy (pages 15-16; 22); thus, enablement of this potential use is also considered with regard to all product claims not specifying a particular use. The specification also discloses the cloning of nucleic acids of the invention and the further study thereof in vectors, host cells and transgenic animals (pages 9-11; 13); however, such general uses (of cloning, preparation of cells, further study, etc.) apply with regard to any nucleic acid and thus are considered general (rather than specific and substantial) uses. Thus, in the present case, enablement of applicant's product claims has been evaluated with regard to their asserted uses in both diagnostic assays and gene therapy.

It is unpredictable as to whether one of skill in the relevant art could actually use applicant's invention in a manner reasonably commensurate with the instant claims. It is first noted that neither the specification nor the prior art provide any evidence that any nucleic acid encompassed by the claims may be successfully employed in any type of gene therapy. Accordingly, enablement is considered as lacking with regard to this asserted use of the products of the claims. Thus, enablement of applicant's invention - both with regard to the product claims and method claims under consideration herein - hinges on the ability of one of skill in the relevant art to employ the nucleic acids and compositions recited in the claims in the diagnosis of lactose intolerance or the predisposition thereto in a manner reasonably commensurate with the claims. The rejected claims broadly encompass many thousands of different nucleic acid molecules sharing only a small region of identify (as few as 14 nucleotides) with the target sequences that must be successfully detected to indicate the presence of lactose intolerance. It is particularly noted that the claims are not directed to, e.g., fragments of SEQ ID NOS 3 and/or 5 that include position 324, or to nucleic acids including position 324 that hybridize to these critical target sequences under highly stringent conditions (as specified above). Rather, the claims embrace sequences of 14, 15, 16, etc., nucleotides from SEQ ID NOs 3/5 that may be flanked on either side by thousands of nucleotides of unrelated sequences. It is noted that the specification at pages 5-6 specifies that the language "nucleic acid molecule…comprising the nucleic acid sequence of SEQ ID NO:" refers to nucleic acids at least 1 nucleotide longer than the SEQ ID NO and extending up to a maximum

of 30,000 nucleotides "over the 5' and/or 3' end of the nucleic acid molecule" specified. However, the instant claims do not employ this particular language, such that the present claims appear to include even larger molecules. Further, even if this language were to be considered limiting, the claims would encompass many thousands of different nucleic acids having only a small region of complementarity with the target sequence whose specific detection is required to achieve a diagnosis. With further regard to applicant's method claims, it is noted that these claims also broadly recite probes having the characteristics noted above, and that the claims are not further limited in any manner with regard to, e.g., the use of conditions that would limit the methods in such a way that one of skill in the art would expect the methods as performed to result in successful diagnosis of lactose intolerance. In contrast to the breadth of the claims, the specification exemplifies the detection of the SNP contained within instant SEQ ID NOs 3/5 (at position 324) using minisequencing and PCR with particular, preferred primers (pages 29-32). Thus, the specification exemplifies the successful use of only a few particular oligonucleotide molecules in the detection of the lactose intolerance associated polymorphism encompassed by SEQ ID NOS 3 and 5. Lacking guidance of the specification, one of skill in the relevant art may look to the teachings of the prior art for further guidance with regard to enablement of a claimed invention. Given the high skill level of such an artisan, it would clearly be within the ability of such a practitioner to design and successfully use other nucleic acid embraced by the claims in the successful detection of lactose intolerance. Particularly, such an artisan could successfully employ any nucleic acid that was sufficiently similar

to the target of interest to allow for the specific detection of and differentiation of the SNP at position 324 of SEQ ID NO: 3/5; such nucleic acids would include fragments of SEQ ID NOs 3/5 that include the SNP, as well as other molecules that hybridize to their target sequences under the highly stringent conditions specified in the specification. However, the vast majority of the nucleic acids molecules and compositions broadly encompassed by the claims do not fall into the category of molecules that could be so employed. Furthermore, it is noted that the nucleic acids, compositions and probe combinations of the claims are free of the prior art, such that the art does not provide any further specific guidance or examples of molecules encompassed by the claims that meet the enablement requirement of 35 USC 112, first paragraph. While claims may encompass some inoperative embodiments (*MPEP* 2164.08(b)), in the instant case, due to the breadth of the claims, one of skill in the relevant art would not expect the majority of the molecules, compositions, and probes of the claims to be usable in the diagnosis of lactose intolerance or the predisposition thereto. For this reason, it would require undue experimentation to use applicant's invention in a manner reasonably commensurate with the claims.

Conclusion

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to DIANA JOHANNSEN whose telephone number is (571)272-0744. The examiner can normally be reached on Monday-Friday, 8:30 am-2:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached at 571/272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Diana B. Johannsen/
Primary Examiner, Art Unit 1634

ALIGNMENT OF SEQ ID NO: 3 WITH Birren et al:

```
RESULT 7
AC016516
LOCUS       AC016516              177067 bp    DNA     linear   HTG 01-APR-2000
DEFINITION  Homo sapiens chromosome 2 clone RP11-329I10 map 2, WORKING DRAFT
            SEQUENCE, 19 unordered pieces.
ACCESSION   AC016516
VERSION     AC016516.3  GI:7381821
KEYWORDS    HTG; HTGS_PHASE1; HTGS_DRAFT.
SOURCE      Homo sapiens (human)
  ORGANISM  Homo sapiens
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini;
            Catarrhini; Hominidae; Homo.
REFERENCE   1  (bases 1 to 177067)
  AUTHORS   Birren,B., Linton,L., Nusbaum,C. and Lander,E.
  TITLE     Homo sapiens chromosome 2, clone RP11-329I10
  JOURNAL   Unpublished
REFERENCE   2  (bases 1 to 177067)
  AUTHORS   Birren,B., Linton,L., Nusbaum,C., Lander,E., Allen,N., Anderson,M.,
            Baldwin,J., Barna,N., Beckerly,R., Boguslavkiy,L., Boukhgalter,B.,
            Brown,A., Castle,A., Colangelo,M., Collins,S., Collymore,A.,
            Cooke,P., DeArellano,K., Dewar,K., Domino,M., Donelan,L., Doyle,M.,
            Ferreira,P., FitzHugh,W., Forrest,C., Funke,R., Gage,D.,
            Galagan,J., Gardyna,S., Grant,G., Hagos,B., Heaford,A., Horton,L.,
            Howland,J.C., Johnson,R., Jones,C., Kann,L., Karatas,A., Klein,J.,
            Lehoczky,J., Lieu,C., Locke,K., Macdonald,P., Marquis,N.,
            McEwan,P., McGurk,A., McKernan,K., McLaughlin,J., Meldrim,J.,
            Morrow,J., Naylor,J., Norman,C.H., O'Connor,T., O'Donnell,P.,
            Peterson,K., Pollara,V., Riley,R., Roy,A., Santos,R., Severy,P.,
            Stange-Thomann,N., Stojanovic,N., Subramanian,A., Talamas,J.,
            Tesfaye,S., Tirrell,A., Vassiliev,H., Vo,A., Wheeler,J., Wu,X.,
            Wyman,D., Ye,W.J., Zimmer,A. and Zody,M.
  TITLE     Direct Submission
  JOURNAL   Submitted (01-DEC-1999) Whitehead Institute/MIT Center for Genome
            Research, 320 Charles Street, Cambridge, MA 02141, USA
COMMENT     On Apr 1, 2000 this sequence version replaced gi:6649384.
            All repeats were identified using RepeatMasker:
            Smit, A.F.A. & Green, P. (1996-1997)
            http://ftp.genome.washington.edu/RM/RepeatMasker.html
            -------------- Genome Center
                Center: Whitehead Institute/ MIT Center for Genome Research
                Center code: WIBR
                Web site: http://www-seq.wi.mit.edu
```

```
    Contact: sequence_submissions@genome.wi.mit.edu
-------------- Project Information
    Center project name: L3746
    Center clone name: 329_I_10
-------------- Summary Statistics
    Sequencing vector: M13; M77815; 100% of reads
    Chemistry: Dye-terminator Big Dye; 100% of reads
    Assembly program: Phrap; version 0.960731
    Consensus quality: 161435 bases at least Q40
    Consensus quality: 169313 bases at least Q30
    Consensus quality: 172791 bases at least Q20
    Insert size: 199000; agarose-fp
    Insert size: 175267; sum-of-contigs
    Quality coverage: 3.9 in Q20 bases; agarose-fp
    Quality coverage: 4.4 in Q20 bases; sum-of-contigs
-------------.
* NOTE: This is a 'working draft' sequence. It currently
* consists of 19 contigs. The true order of the pieces
* is not known and their order in this sequence record is
* arbitrary. Gaps between the contigs are represented as
* runs of N, but the exact sizes of the gaps are unknown.
* This record will be updated with the finished sequence
* as soon as it is available and the accession number will
* be preserved.
*       1     1456: contig of 1456 bp in length
*     1457     1556: gap of 100 bp
*     1557     2853: contig of 1297 bp in length
*     2854     2953: gap of 100 bp
*     2954     5239: contig of 2286 bp in length
*     5240     5339: gap of 100 bp
*     5340     7298: contig of 1959 bp in length
*     7299     7398: gap of 100 bp
*     7399    10019: contig of 2621 bp in length
*    10020    10119: gap of 100 bp
*    10120    12837: contig of 2718 bp in length
*    12838    12937: gap of 100 bp
*    12938    15695: contig of 2758 bp in length
*    15696    15795: gap of 100 bp
*    15796    23564: contig of 7769 bp in length
*    23565    23664: gap of 100 bp
*    23665    29299: contig of 5635 bp in length
*    29300    29399: gap of 100 bp
*    29400    41595: contig of 12196 bp in length
*    41596    41695: gap of 100 bp
*    41696    53365: contig of 11670 bp in length
*    53366    53465: gap of 100 bp
*    53466    63384: contig of 9919 bp in length
*    63385    63484: gap of 100 bp
*    63485    74107: contig of 10623 bp in length
*    74108    74207: gap of 100 bp
*    74208    85566: contig of 11359 bp in length
*    85567    85666: gap of 100 bp
*    85667    96308: contig of 10642 bp in length
*    96309    96408: gap of 100 bp
```

```
            *    96409   103702: contig of 7294 bp in length
            *   103703   103802: gap of 100 bp
            *   103803   113924: contig of 10122 bp in length
            *   113925   114024: gap of 100 bp
            *   114025   130434: contig of 16410 bp in length
            *   130435   130534: gap of 100 bp
            *   130535   177067: contig of 46533 bp in length.
FEATURES             Location/Qualifiers
     source          1. .177067
                     /organism="Homo sapiens"
                     /mol_type="genomic DNA"
                     /db_xref="taxon:9606"
                     /chromosome="2"
                     /map="2"
                     /clone="RP11-329I10"
                     /clone_lib="RPCI-11 Human Male BAC"
     misc_feature    1. .1456
                     /note="assembly_fragment"
     gap             1457. .1556
                     /estimated_length=100
     misc_feature    1557. .2853
                     /note="assembly_fragment"
     gap             2854. .2953
                     /estimated_length=100
     misc_feature    2954. .5239
                     /note="assembly_fragment"
     gap             5240. .5339
                     /estimated_length=100
     misc_feature    5340. .7298
                     /note="assembly_fragment"
     gap             7299. .7398
                     /estimated_length=100
     misc_feature    7399. .10019
                     /note="assembly_fragment"
     gap             10020. .10119
                     /estimated_length=100
     misc_feature    10120. .12837
                     /note="assembly_fragment"
     gap             12838. .12937
                     /estimated_length=100
     misc_feature    12938. .15695
                     /note="assembly_fragment"
     gap             15696. .15795
                     /estimated_length=100
     misc_feature    15796. .23564
                     /note="assembly_fragment"
     gap             23565. .23664
                     /estimated_length=100
     misc_feature    23665. .29299
                     /note="assembly_fragment"
     gap             29300. .29399
                     /estimated_length=100
     misc_feature    29400. .41595
                     /note="assembly_fragment"
```

```
     gap             41596. .41695
                     /estimated_length=100
     misc_feature    41696. .53365
                     /note="assembly_fragment"
     gap             53366. .53465
                     /estimated_length=100
     misc_feature    53466. .63384
                     /note="assembly_fragment"
     gap             63385. .63484
                     /estimated_length=100
     misc_feature    63485. .74107
                     /note="assembly_fragment"
     gap             74108. .74207
                     /estimated_length=100
     misc_feature    74208. .85566
                     /note="assembly_fragment"
     gap             85567. .85666
                     /estimated_length=100
     misc_feature    85667. .96308
                     /note="assembly_fragment"
     gap             96309. .96408
                     /estimated_length=100
     misc_feature    96409. .103702
                     /note="assembly_fragment"
     gap             103703. .103802
                     /estimated_length=100
     misc_feature    103803. .113924
                     /note="assembly_fragment
                     clone_end:SP6
                     vector_side:right"
     gap             113925. .114024
                     /estimated_length=100
     misc_feature    114025. .130434
                     /note="assembly_fragment"
     gap             130435. .130534
                     /estimated_length=100
     misc_feature    130535. .177067
                     /note="assembly_fragment
                     clone_end:T7
                     vector_side:right"
ORIGIN

  Query Match             93.7%;  Score 3009;  DB 12;  Length 177067;
  Best Local Similarity   99.9%;  Pred. No. 0;
  Matches 3209;  Conservative    0;  Mismatches    4;  Indels    0;  Gaps    0;

Qy          1 ATCAGAGTCACTTTGATATGATGAGAGCAGAGATAAACAGATTTGTTGCATGTTTTTAAT 60
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      81692 ATCAGAGTCACTTTGATATGATGAGAGCAGAGATAAACAGATTTGTTGCATGTTTTTAAT 81751

Qy         61 CTTTGGTATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGC 120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      81752 CTTTGGTATGGGACATACTAGAATTCACTGCAAATACATTTTTATGTAACTGTTGAATGC 81811
```

```
Qy        121 TCATACGACCATGGAATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTT 180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      81812 TCATACGACCATGGAATTCTTCCCTTTAAAGAGCTTGGTAAGCATTTGAGTGTAGTTGTT 81871

Qy        181 AGACGGAGACGATCACGTCATAGTTTATAGAGTGCATAAAGACGTAAGTTACCATTTAAT 240
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      81872 AGACGGAGACGATCACGTCATAGTTTATAGAGTGCATAAAGACGTAAGTTACCATTTAAT 81931

Qy        241 ACCTTTCATTCAGGAAAAATGTACTTAGACCCTACAATGTACTAGTAGGCCTCTGCGCTG 300
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      81932 ACCTTTCATTCAGGAAAAATGTACTTAGACCCTACAATGTACTAGTAGGCCTCTGCGCTG 81991

Qy        301 GCAATACAGATAAGATAATGTAGTCCCTGGCCTCAAAGGAACTCTCCTCCTTAGGTTGCA 360
              |||||||||||||||||||||| ||||||||||||||||||||||||||||||||||||||
Db      81992 GCAATACAGATAAGATAATGTAGCCCCTGGCCTCAAAGGAACTCTCCTCCTTAGGTTGCA 82051

Qy        361 TTTGTATAATGTTTGATTTTTAGATTGTTCTTTGAGCCCTGCATTCCACGAGGATAGGTC 420
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82052 TTTGTATAATGTTTGATTTTTAGATTGTTCTTTGAGCCCTGCATTCCACGAGGATAGGTC 82111

Qy        421 AGTGGGTATTAACGAGGTAAAAGGGGAGTAGTACGAAAGGGCATTCAAGCGTCCCATCTT 480
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82112 AGTGGGTATTAACGAGGTAAAAGGGGAGTAGTACGAAAGGGCATTCAAGCGTCCCATCTT 82171

Qy        481 CGCTTCAACCAAAGCAGCCCTGCGTTTTCCTAGTTTTATTAATAGGTTTGATGTAAGGTC 540
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82172 CGCTTCAACCAAAGCAGCCCTGCGTTTTCCTAGTTTTATTAATAGGTTTGATGTAAGGTC 82231

Qy        541 GTCTTTGAAAAGGGGGTTTGGCTTTTTTTTACAGTGTGACTGAGGTATAATTTATAAAAA 600
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82232 GTCTTTGAAAAGGGGGTTTGGCTTTTTTTTACAGTGTGACTGAGGTATAATTTATAAAAA 82291

Qy        601 GGGAAATGTATGGCATGGTGAGTTTTTTCACATACATCCTTGTGAATACCCAGCTCAAGA 660
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82292 GGGAAATGTATGGCATGGTGAGTTTTTTCACATACATCCTTGTGAATACCCAGCTCAAGA 82351

Qy        661 TCCAAAACATTTCCATAATTTCAGAAAGTTCCAAACCCCTGCCTCTTTTCAGTCTTAGCC 720
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82352 TCCAAAACATTTCCATAATTTCAGAAAGTTCCAAACCCCTGCCTCTTTTCAGTCTTAGCC 82411

Qy        721 CTCTTCCCCTGAAGTAACCACTGTTCCGACTTCAATCACTACTTTTATCCCACAGGTTAA 780
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82412 CTCTTCCCCTGAAGTAACCACTGTTCCGACTTCAATCACTACTTTTATCCCACAGGTTAA 82471

Qy        781 TTTTTTGGCTTTTTTCCACTAAATTTTCAAATTCTTTGATATGGTACTTTACTATTGACG 840
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82472 TTTTTTGGCTTTTTTCCACTAAATTTTCAAATTCTTTGATATGGTACTTTACTATTGACG 82531

Qy        841 AAGTACTTTCACACTAGGTTATTTAATATTCTTTGATTCACCCAATATTTAGGGAACACC 900
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82532 AAGTACTTTCACACTAGGTTATTTAATATTCTTTGATTCACCCAATATTTAGGGAACACC 82591

Qy        901 TGTAGGGGACAAAAAATGAATGAGAGCCCCTGCCTTCCATTGCTGCTAATCTGGTGGGAA 960
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db      82592 TGTAGGGGACAAAAAATGAATGAGAGCCCCTGCCTTCCATTGCTGCTAATCTGGTGGGAA 82651

Qy        961 CGAGACATGTATTTAATTAAGCATGTAAAAAATAGAGTGGGTGATGAAATAATCTATATA 1020
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82652 CGAGACATGTATTTAATTAAGCATGTAAAAAATAGAGTGGGTGATGAAATAATCTATATA 82711

Qy       1021 CTAAATCCCCATGACACACAGTTTACCTATGTAACAAACCTGCATGTGTACCCCCGAACC 1080
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82712 CTAAATCCCCATGACACACAGTTTACCTATGTAACAAACCTGCATGTGTACCCCCGAACC 82771

Qy       1081 TAAAATATAAGTTGGAAATTAAAAAAAAACGAGAGGGAGAATAGAGCATCACAACCAGAG 1140
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82772 TAAAATATAAGTTGGAAATTAAAAAAAAACGAGAGGGAGAATAGAGCATCACAACCAGAG 82831

Qy       1141 TGCTGAGATGAATTACTTTATTACCAAAGAAGGAGGAGGACTCAGGGAGGTGCCGACGTT 1200
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82832 TGCTGAGATGAATTACTTTATTACCAAAGAAGGAGGAGGACTCAGGGAGGTGCCGACGTT 82891

Qy       1201 TAAACCCAGTCACTGAAGGGTGTGCAGAATTTGGATAGGCAAGATACCCTGGGACAAGGT 1260
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82892 TAAACCCAGTCACTGAAGGGTGTGCAGAATTTGGATAGGCAAGATACCCTGGGACAAGGT 82951

Qy       1261 CATTCTAAAACCATGCTAACATTTGTACTTTTTTTTTCATTGTGATAGTTCCTGAAATGA 1320
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      82952 CATTCTAAAACCATGCTAACATTTGTACTTTTTTTTTCATTGTGATAGTTCCTGAAATGA 83011

Qy       1321 GTTGCATAAAACTGGTACATGTCTTAGGGCAGTCTCTAATTGATTTTTATTTTGTTCTAT 1380
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83012 GTTGCATAAAACTGGTACATGTCTTAGGGCAGTCTCTAATTGATTTTTATTTTGTTCTAT 83071

Qy       1381 TTTTAAAAATTAGTCTTCAAATAGCAGATTCACATGATATTAAAATATATGCACATAAAT 1440
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83072 TTTTAAAAATTAGTCTTCAAATAGCAGATTCACATGATATTAAAATATATGCACATAAAT 83131

Qy       1441 TATATACACAAATATATTTTCTGAATGAAATTTAGTATCTGCATATATTTAAGAGCTATT 1500
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83132 TATATACACAAATATATTTTCTGAATGAAATTTAGTATCTGCATATATTTAAGAGCTATT 83191

Qy       1501 TCTGTCTCATATGTTCATAATCTTCATCCATTAAAAAAACTTTTGTTAGGCCTTTCTCAC 1560
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83192 TCTGTCTCATATGTTCATAATCTTCATCCATTAAAAAAACTTTTGTTAGGCCTTTCTCAC 83251

Qy       1561 TCTAAGATTATAAAAAATTCTCCCATTATTTACCTAGCTAGTTTTCTAGTTGTTCCAAAA 1620
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83252 TCTAAGATTATAAAAAATTCTCCCATTATTTACCTAGCTAGTTTTCTAGTTGTTCCAAAA 83311

Qy       1621 CCATTTATTGAACAATCCATCTTTTTGACACTGGTTTGGCATGCCTTAATTATATATTCT 1680
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83312 CCATTTATTGAACAATCCATCTTTTTGACACTGGTTTGGCATGCCTTAATTATATATTCT 83371

Qy       1681 TGTGTGTGTTAGGATCTCCTTTTGGACTTTCCATTCTGTTCATTGAGTCTTATCAGCTCC 1740
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83372 TGTGTGTGTTAGGATCTCCTTTTGGACTTTCCATTCTGTTCATTGAGTCTTATCAGCTCC 83431
```

```
Qy       1741 TCTTACATTGGTACCATGATGTTTTAATCTATGGGGCTTTGTAGTTTAAATGTAGGGCTA 1800
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83432 TCTTACATTGGTACCATGATGTTTTAATCTATGGGGCTTTGTAGTTTAAATGTAGGGCTA 83491

Qy       1801 GTTCCAGCGCATTGTTCTCTATCAGCTGTTAGGAACTTAGAAATCAGCTTGCTCTGTTTT 1860
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83492 GTTCCAGCGCATTGTTCTCTATCAGCTGTTAGGAACTTAGAAATCAGCTTGCTCTGTTTT 83551

Qy       1861 AAAGAAAAACCTGGTATTTTTTTATCAGTATAACATTCTATTTATATTAACTTGAAGAAT 1920
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83552 AAAGAAAAACCTGGTATTTTTTTATCAGTATAACATTCTATTTATATTAACTTGAAGAAT 83611

Qy       1921 TGAAAACATCTATGATTTTTCCTATTCAGTAACGTATCACTTAGAATAGGTTAGGTTGTA 1980
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83612 TGAAAACATCTATGATTTTTCCTATTCAGTAACGTATCACTTAGAATAGGTTAGGTTGTA 83671

Qy       1981 CTACTATAAAATCTCAGCTGCATAAAACAATTTTTTTTTGCTTGTGCTACACATCCATTA 2040
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83672 CTACTATAAAATCTCAGCTGCATAAAACAATTTTTTTTTGCTTGTGCTACACATCCATTA 83731

Qy       2041 GGTCATCAAGGGACTCACCTTGTCAAGTTACTCAGAGATTCAGGCTGATATAAAGGTTTG 2100
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83732 GGTCATCAAGGGACTCACCTTGTCAAGTTACTCAGAGATTCAGGCTGATATAAAGGTTTG 83791

Qy       2101 ATCTTGACATACGCTTTCATGATGACAGAAAGCAGGGAAGAGAAGGTGGTGAGCCATGTG 2160
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83792 ATCTTGACATACGCTTTCATGATGACAGAAAGCAGGGAAGAGAAGGTGGTGAGCCATGTG 83851

Qy       2161 CTTTCTCCCCCTTCTATCCAGAAATGACACATACTCACATTTCATTCGCCAGAGAAATTA 2220
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83852 CTTTCTCCCCCTTCTATCCAGAAATGACACATACTCACATTTCATTCGCCAGAGAAATTA 83911

Qy       2221 ACATGGCCCCTCCTAAGTTCAAATGGATAGAGAAATGCCTTCCTACCAGGTGCCCAGAAT 2280
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83912 ACATGGCCCCTCCTAAGTTCAAATGGATAGAGAAATGCCTTCCTACCAGGTGCCCAGAAT 83971

Qy       2281 TAGAAGAGCAAACATTTGTGAACAGTTCTGAGTACCACAAATACCGTTATCTTTCCACTT 2340
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      83972 TAGAAGAGCAAACATTTGTGAACAGTTCTGAGTACCACAAATACCGTTATCTTTCCACTT 84031

Qy       2341 AAGTCTTCTGTTTCACTCAGTAGTGCTTTAAACTTTTCTTCATATGTTTTTCAGTGTTTC 2400
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84032 AAGTCTTCTGTTTCACTCAGTAGTGCTTTAAACTTTTCTTCATATGTTTTTCAGTGTTTC 84091

Qy       2401 TTGTTGAATTTCTTGATATTTTATCATGTTTGTTCGTACTGGGAGTAGCCTTTTTTTCCA 2460
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84092 TTGTTGAATTTCTTGATATTTTATCATGTTTGTTCGTACTGGAAGTAGCCTTTTTTTCCA 84151

Qy       2461 TTTCATTTTCTGGCTGGTTTCATTGCTGGTTGTTTTTTTGTTTTGTTTTGTTTTTGAGAT 2520
             |||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84152 TTTCATTTTCTGGCTGGTTTCATTGCTGATTGTTTTTTTGTTTTGTTTTGGTTTTGAGAT 84211

Qy       2521 GGAGTCTCACTCTGTCGCCCAGGCTGGAGTGCAGTGTCACAATCTCGGCTCACTGCAACC 2580
             ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
```

```
Db      84212 GGAGTCTCACTCTGTCGCCCAGGCTGGAGTGCAGTGTCACAATCTCGGCTCACTGCAACC 84271

Qy       2581 TCTGCCTCCCAGGTTCAAGCGATTCTTCTTTCTCAGCCTCCTGAGTAGCTGGGATTACAG 2640
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84272 TCTGCCTCCCAGGTTCAAGCGATTCTTCTTTCTCAGCCTCCTGAGTAGCTGGGATTACAG 84331

Qy       2641 GCATGTGCCACCATGCCCAGCTAATTTTTTATATTTTTAGTAGAGATGGGGTTTCTCCAT 2700
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84332 GCATGTGCCACCATGCCCAGCTAATTTTTTATATTTTTAGTAGAGATGGGGTTTCTCCAT 84391

Qy       2701 GTTGGTCAGGCTGGTCTCAAACTCCCAATCTCAGGTGATCCGCCTGCCTCTGCCTTCCAA 2760
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84392 GTTGGTCAGGCTGGTCTCAAACTCCCAATCTCAGGTGATCCGCCTGCCTCTGCCTTCCAA 84451

Qy       2761 AGTGCTGGGATTATAGACATGAGCCACCGTGCCTGGCCTAGTTCTTATGGGATGTATATG 2820
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84452 AGTGCTGGGATTATAGACATGAGCCACCGTGCCTGGCCTAGTTCTTATGGGATGTATATG 84511

Qy       2821 TCTTTGGATTCATATGATATGTATATATGTTTATATTTCTACAAGTACATACCTAGGAGT 2880
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84512 TCTTTGGATTCATATGATATGTATATATGTTTATATTTCTACAAGTACATACCTAGGAGT 84571

Qy       2881 GGAATTGTTGGGTCATAGGTTAATGCATGTTTTTCTGCCAAACAGTTGTGTCAATTTCTG 2940
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84572 GGAATTGTTGGGTCATAGGTTAATGCATGTTTTTCTGCCAAACAGTTGTGTCAATTTCTG 84631

Qy       2941 TTTTCACCGCTGTGAATGAGAGTTGTTCTACCTTCTTGACAACACTTGATATTGTCAGTC 3000
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84632 TTTTCACCGCTGTGAATGAGAGTTGTTCTACCTTCTTGACAACACTTGATATTGTCAGTC 84691

Qy       3001 ATTTTAGCCATTCTGGTGAATTTATAGTGCTATTTCTGTGTGTGTAAGAGAGAGAATGAG 3060
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84692 ATTTTAGCCATTCTGGTGAATTTATAGTGCTATTTCTGTGTGTGTAAGAGAGAGAATGAG 84751

Qy       3061 AGAGGGTGTTTGTGAGAAAACCAAAGCAACACTGTGAGAGTGTGTGTGTTTGTGAGAAAA 3120
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84752 AGAGGGTGTTTGTGAGAAAACCAAAGCAACACTGTGAGAGTGTGTGTGTTTGTGAGAAAA 84811

Qy       3121 CCAAAATACATACTACTGTGATTTCATTGGGAGAAAATCTGTTTGGTATATCAAAAAAAG 3180
              ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      84812 CCAAAATACATACTACTGTGATTTCATTGGGAGAAAATCTGTTTGGTATATCAAAAAAAG 84871

Qy       3181 TAGCTTAATTACTTCATCATTATTGGTTTAGGT 3213
              |||||||||||||||||||||||||||||||||
Db      84872 TAGCTTAATTACTTCATCATTATTGGTTTAGGT 84904
```